

Enteric Coating and Stability of Aqueous Enteric Systems on HPMC Capsules

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Introduction

The formulation of drugs into capsules is often utilized in early phase development due to the relatively quicker formulation-development process. The bioavailability of the poorly soluble drugs can be significantly increased when formulated in a solubilized form in a capsule (i.e. liquid or semi-solid filled capsules). Acidic degradation and dyspeptic side effects associated with some compounds are overcome by enteric coating of the dosage form. This work is an evaluation of the ability of commercially available enteric, aqueous film-coating systems to confer their enteric release properties on hydroxypropyl methylcellulose (HPMC) capsules.

Objectives

To develop a robust enteric coating process for HPMC capsules using Cellulose Acetate Phthalate (Aquacoat® CPD) and Polyvinyl Acetate Phthalate (Sureteric®) coating systems and to evaluate the stability of the enteric coated HPMC capsules.

Methods

Capsule Coating

Size 0 HPMC capsules (Capsugel®) were filled with anhydrous lactose, NF (Kerry Bio-Science) using a hand-held Feton® encapsulator. One liter of filled capsules were enteric coated with either Aquacoat® CPD (FMC BioPolymer) or Sureteric® (Colorcon) over a base coat of Opadry® (Colorcon) using a LDSC 5 Hi-Coater® (Vector Corporation) with a 1.3L (9.5") partially perforated coating pan. Capsules were coated to a target coating level of 12 mg/cm² (surface area of size 0 capsule ~5 cm²). Capsules coated at 75% of the target level were collected for evaluation.

Table 1: Formulation and Process Parameters

Coating System Formulations	Sureteric®	Aquacoat® CPD
Sub-Coat	Opadry®, Clear 15% (w/w) in Water	Not Applicable
Target Coating level (mg/cm ²)	2	
Process Time (Minutes)	25	
Enteric Coat	Sureteric® 15% (w/w) in Water with 0.05% Antifoam C Emulsion (Dow Corning®)	Aquacoat CPD 40% (w/w) in Water with 2.9% (w/w) Triethyl Citrate
Target Coating level (mg/cm ²)	12	12
Process Time (Minutes)	90	75
Process		
Sub-Coat		
Inlet Temperature (°C)	60	
Exhaust Temperature (°C)	38-40	
Bed Temperature (°C)	34-36	
Air Volume (CFM)	20	
Spray Rate (g/min.)	3	
Pan Speed (RPM)	12	
Enteric Coat		
Inlet Temperature (°C)	60	60
Exhaust Temperature (°C)	38-43	36-40
Bed Temperature (°C)	35-36	32-36
Air Volume (CFM)	20	20
Spray Rate (g/min.)	3-4	5
Pan Speed (RPM)	12	12

Scanning Electron Microscopy (SEM)

SEM (Hitachi S-800) images were obtained to assess how well the coating materials covered the junction between the capsule body and cap.

Stability Packaging and Storage

30 coated capsules or uncoated capsules were added into 100cc white HDPE bottles with a 1g silica-gel desiccant before capping and inductions sealing. Packaged capsules were placed on stability storage at 40°C/75% relative humidity (RH) for evaluation at initial, 1, 2, and 3 months time points. Samples were placed at 25°C/60%RH for contingency testing in the event of 40°C/75%RH storage samples failure.

Disintegration Testing

The efficacy of the enteric coatings was evaluated by disintegration testing as per USP <701> procedure for delayed-release (enteric-coated) tablets.

Capsule Fill Moisture Content

Initially and at each stability time-point the anhydrous lactose capsule fill of the coated and uncoated capsules was assayed for water per USP <921> Water Determination method 1a (direct titration). For each coating material, water determinations were performed on the combined contents of three capsules from the 75% (9 mg/cm²) and the 100% (12 mg/cm²) coating levels after 1 hour disintegration testing in USP Simulated Gastric Fluid (SGF) Test Solution to assess gastric media intrusion into the capsules.

Results

SEM images of the coated capsules' surfaces (Figure 1) reveal differences in coating texture and coverage at the body/cap junction. Aquacoat® CPD coated capsules displayed a visible gap at the body/cap junction while the Sureteric® film coat appeared to bridge this gap.

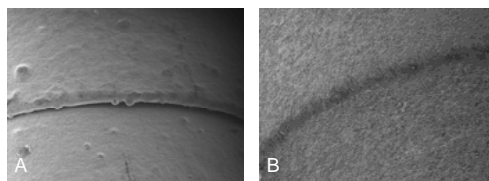


Figure 1: A) Capsule coated with Aquacoat® CPD (12 mg/cm²)
B) Capsule coated with Sureteric® (12 mg/cm²) over a base coat of Opadry® (2 mg/cm²)

Disintegration testing showed the two coating materials to be effective as enteric coating agents on the HPMC capsules. Both coating materials kept the capsules intact during disintegration testing in SGF and release in USP Simulated Intestinal Fluid (SIF) Test Solution occurred from the domed ends of the capsules. Table 2 below shows the disintegration times of the capsules in SIF subsequent to 1 hour of disintegration testing in SGF.

Table 2: Disintegration Times of 40°C/75% RH Stability Storage Samples in SIF

Sample	Initial	T=1 Month	T=2 Months	T=3 Months
Aquacoat® CPD Coated Capsules	15 min. 10 sec.	27 min. 18 sec.	17 min. 44 sec.	20 min. 44 sec.
Sureteric® Coated Capsules	20 min. 21 sec.	39 min. 6 sec.	26 min. 30 sec.	34 min. 21 sec.
Uncoated Capsules	Disintegrated in SGF			

Upon testing the water content of the capsule fill from capsules after 1 hour of disintegration testing in SGF, it was noted that the Aquacoat® CPD coated capsules were weak and easily broken in half at the cap/body junction. The Sureteric® coated capsules tested remained rigid and had to be cut open after 1 hour testing in SGF. Table 3 below shows the moisture content of the capsule fill from stability storage samples and compares the water content of capsules coated at the 75% and 100% levels after 1 hour of disintegration testing in SGF.

Table 3: Moisture Content of Capsule Fill Material (%weight)

Sample	Initial	1-1 Month At 40°C/75%RH	1-2 Months At 40°C/75%RH	1-3 Months At 40°C/75%RH	75% Coating Level After 1 Hour in SGF	100% Coating Level After 1 Hour in SGF
Aquacoat® CPD Coated Capsules	0.97	0.96	0.92	0.95	3.30	1.35
Sureteric® Coated Capsules	0.96	1.03	0.96	0.97	2.93	1.34
Uncoated Capsules	0.96	1.02	1.09	1.05	Not Performed	

The data in Table 3 above demonstrates that the capsule fill had no significant increase in moisture content during stability storage and that both coating materials provided approximately the same protection from gastric media at comparable coating levels.

Conclusions

It has been demonstrated that the enteric coating process developed for HPMC capsules is robust, stable, and similar to enteric coating of tablets.

References

1. FMC BioPolymer. "Aquacoat," Retrieved on November 04, 2008, from <http://www.fmcbiopolymer.com/Products/Aquacoat/tabid/2945/Default.aspx>
2. Colorcon. "Sureteric® Aqueous Enteric Coating System," Retrieved on November 04, 2008, from <http://www.colorcon.com/products/coatings/enteric-delayed-release/sureteric/Product%20Overview>